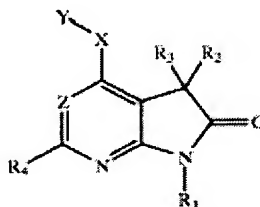


Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently Amended) A compound of Formula 1



or a pharmaceutically acceptable salt, solvate, clathrate, or prodrug thereof, wherein:

R₁ is H or methyl;

each of R₂ and R₃ is independently H, halogen, (C₁-C₃)alkyl, or (C₁-C₃)alkoxy; or R₂ and R₃ taken together form an optionally substituted methyldiene or a 3- to 7-membered ring optionally comprising 0-3 heteroatoms;

R₄ is H, methyl, trifluoromethyl, (C₁-C₄)alkyl, alkoxy, amido, amino, or optionally substituted aryl;

X is a chemical bond, ethynyl, -O-, -S-, -S(O)-, -S(O₂)-, -NR₅C(O)-, or -NR₅-, wherein R₅ is H, methyl, or substituted methylene;

Y is a 5- to 10-membered mono or bicyclic, saturated, unsaturated, or aromatic ring comprising 0-3 heteroatoms and optionally substituted; and

Z is N or CR₆, wherein R₆ is H, halogen, nitro, cyano, alkoxyl, sulfonamide, amino, or amide.

2. (Original) The compound of claim 1 wherein X is a chemical bond, -O-, -S-, or -NR₅-.

3. (Original) The compound of claim 1 wherein Y is selected from the group consisting of phenyl, indolyl, indolinyl, 1H-indazolyl, 2,3-dihydro-1H-indazolyl, 1H-

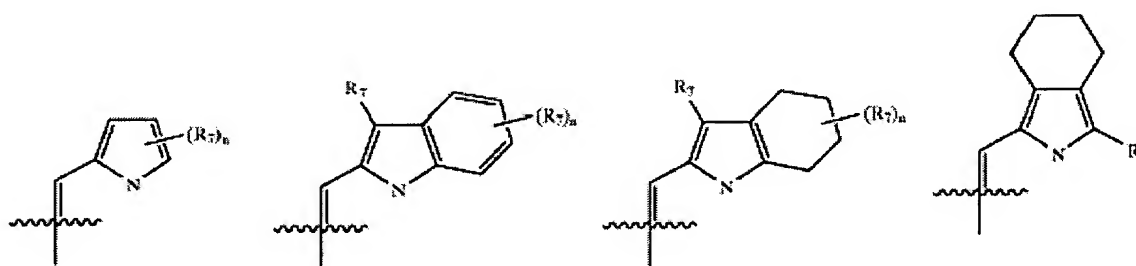
benzimidazolyl, 2,3-dihydro-1H-benzimidazolyl, benzotriazolyl, pyridyl, pyrimidyl, 4-substituted piperazin-1-yl, morpholino, piperidinyl, pyrrolidin-1-yl, furanyl, thiophenyl, pyrrolyl, pyrazolyl, imidazolyl, pyridopyrrolyl, pyridazopyrrolyl, pyrimidopyrrolyl, pyrazopyrrolyl, pyridofuranyl, and derivatives thereof.

4. (Cancelled)

5. (Original) The compound of claim 1 wherein R_2 and R_3 are both H, halogen, or methyl.

6. (Original) The compound of claim 1 wherein R_2 and R_3 are taken together to form a ring selected from the group consisting of 1,3-dioxolane, 1,3-dioxane, cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

7. (Original) The compound of claim 1 wherein R_2 and R_3 are taken together to form an optionally substituted methyindene selected from those of Formulas 1a-1n:

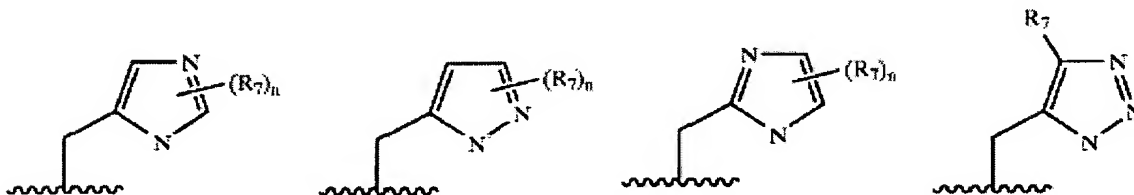


1a

1b

1c

1d

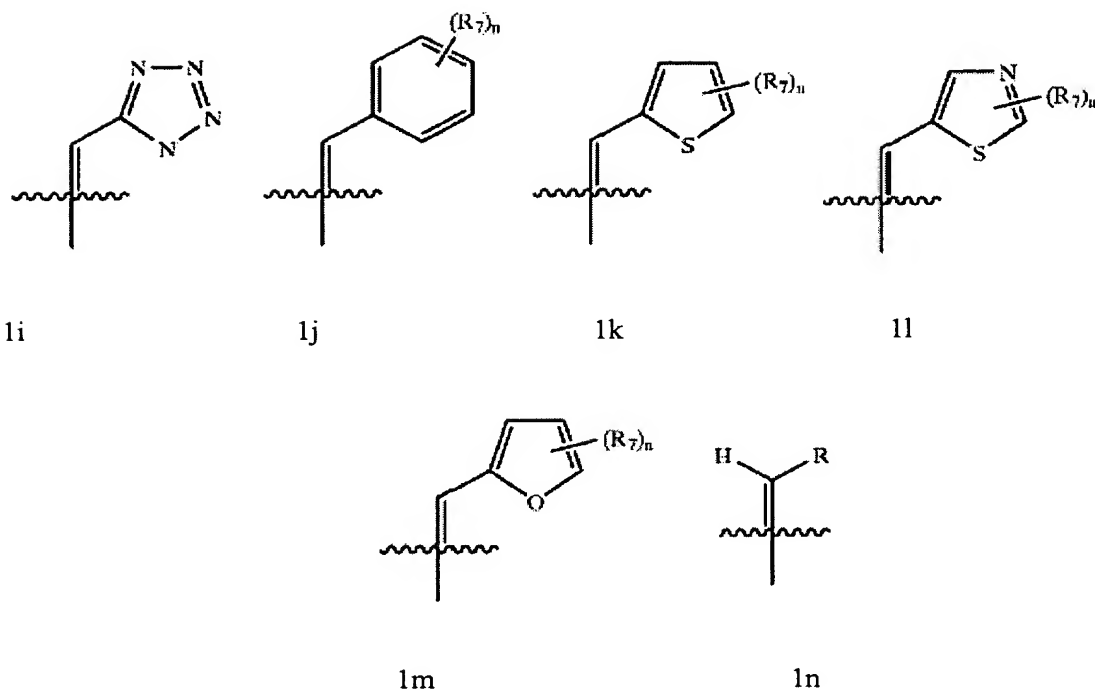


1e

1f

1g

1h



wherein:

n is an integer of 0-3;

each R_7 is independently H, alkyl, carboxylic acid, amine, halogen, nitro, cyano, X_1 , X_2 -(C-C₄)alkyl- R_8 , X_2 -(C₁-C₄)alkenyl- R_8 , or X_2 -(C₁-C₄)alkynyl- R_8 ;

X_1 is -C(O)NR₉-, -NR₉C(O)-, -C(O)O-, C(O)R₁₁-, -OC(O)-, -O-, -NR₉-, -S-, -S(O₂), or -S(O₂)NR₉-;

X_2 is a chemical bond, -C(O)NR₉-, -NR₉C(O)-, -C(O)O-, C(O)R₁₁-, -OC(O)-, -O-, -NR₉-, -S-, -S(O₂), or -S(O₂)NR₉-;

R_8 is selected from the group consisting of hydrogen, dialkylamino, carboxyl, hydroxyl, alkoxy, sulfonamide, urea, carbamate, diol, alkylsulphonyl, and R_{10} ;

R_9 is H or (C₁-C₃)alkyl;

R_{10} is an optionally substituted 5- or 6-membered saturated, unsaturated, or aromatic heterocycle comprising from 1 to 4 heteroatoms; and

R_{11} , is an optionally substituted 5- to 6-membered saturated heterocyclic ring.

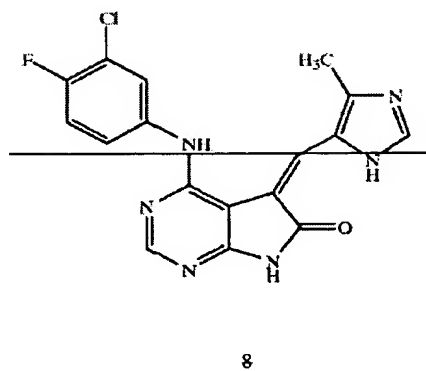
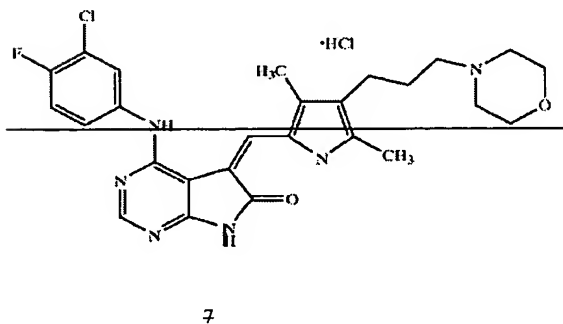
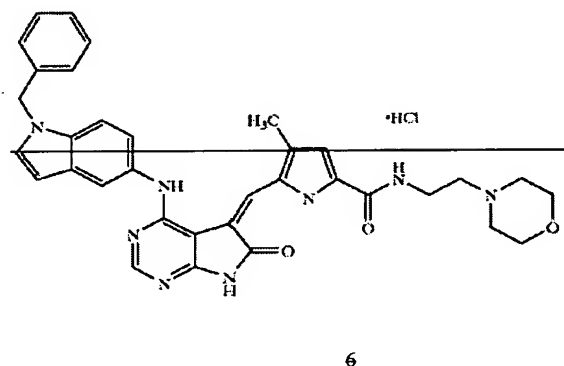
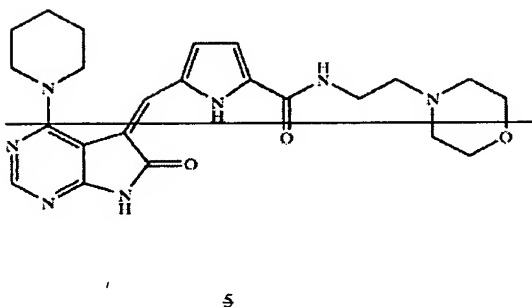
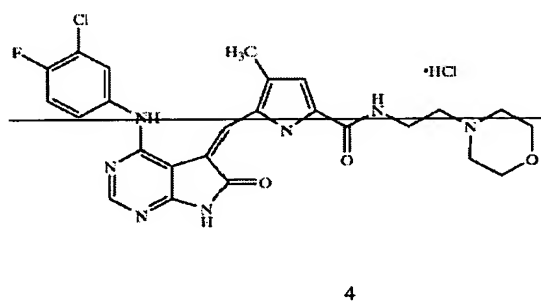
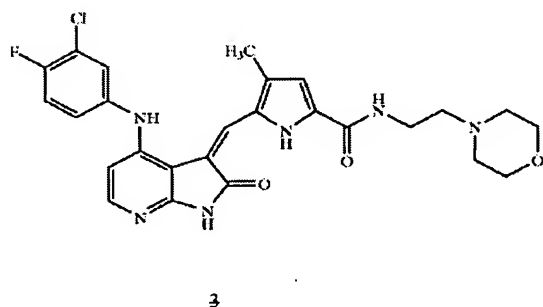
8. (Original) The compound of claim 7 wherein R_7 is X_2 -(C₁-C₄)alkyl- R_8 , X_2 -(C₁-C₄)alkenyl- R_8 , or X_2 -(C₁-C₄)alkynyl- R_8 , and R_8 is selected from the group consisting

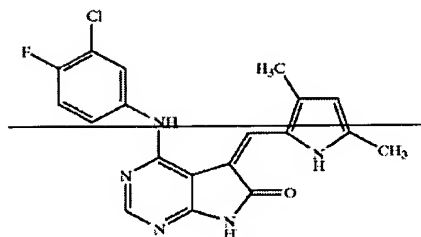
of alkylsulfonyl, alkoxy, carboxyl, morpholino, 1-alkyl-piperazin-4-yl, pyrrolidinyl, piperidinyl, pyridyl, imidazolo, triazolo, tetrazolo, and thiazolo.

9. (Original) The compound of claim 1 wherein R_4 is H, methyl, or trifluoromethyl.

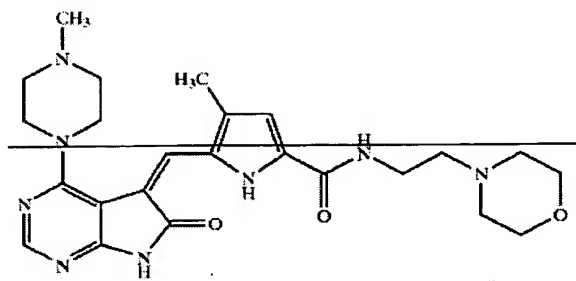
10. (Original) The compound of claim 1 wherein if Z is CH, R_1 is CH_3 or R_3 and R_2 do not form an optionally substituted methylindene.

11. (Currently Amended) A compound selected from the group consisting of:

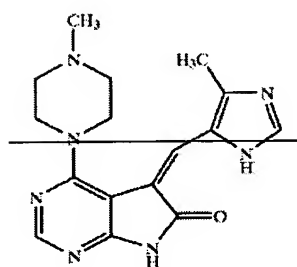




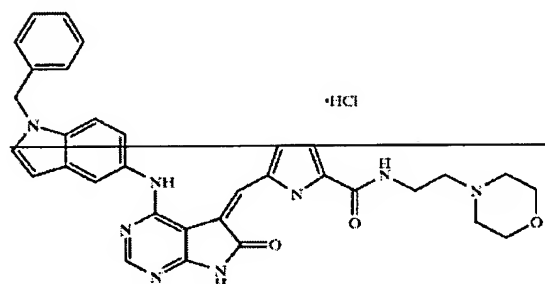
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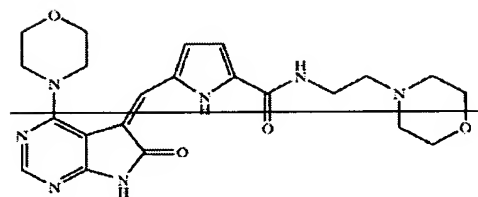
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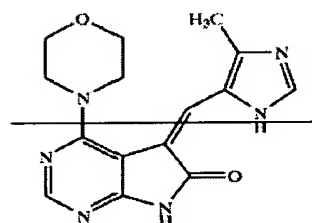
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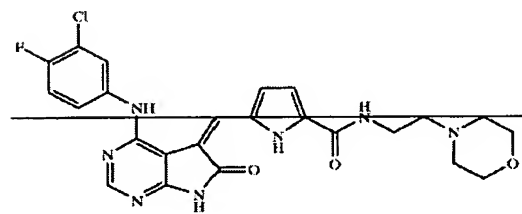
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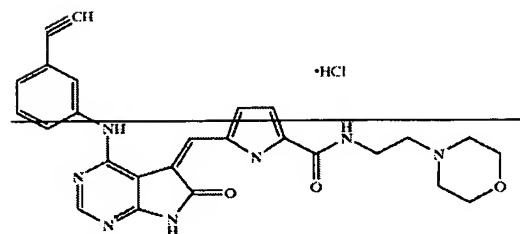
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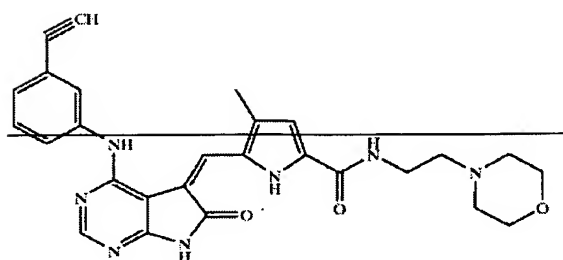
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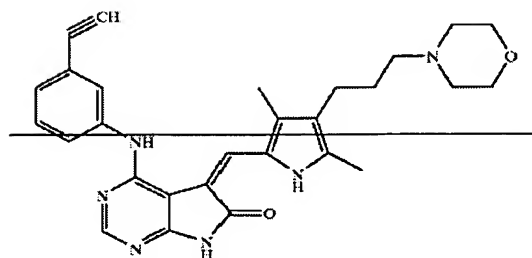
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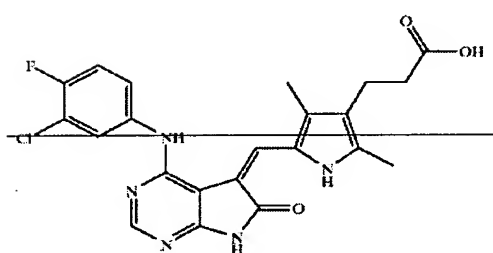
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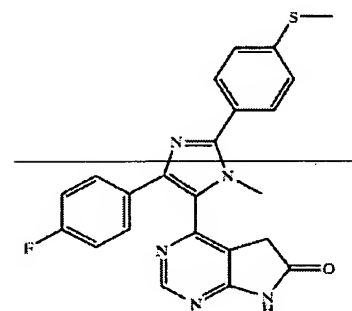
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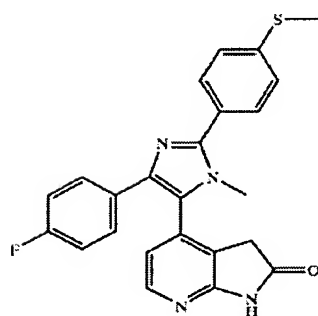
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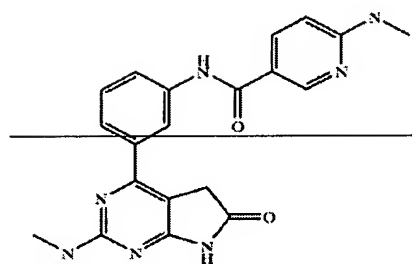
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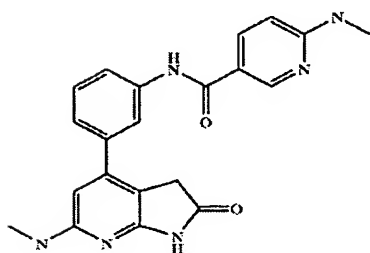
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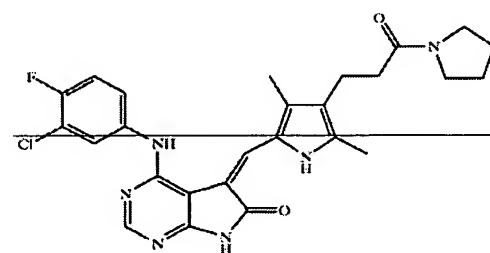
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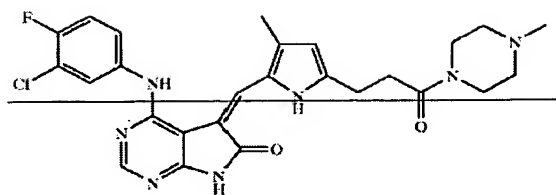
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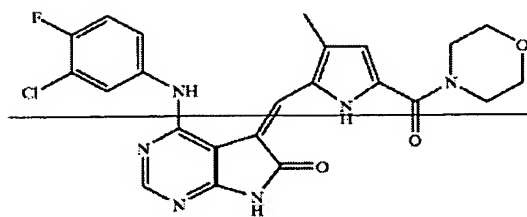
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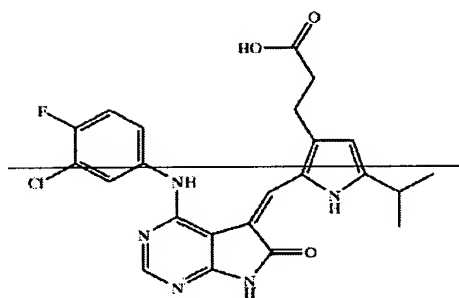
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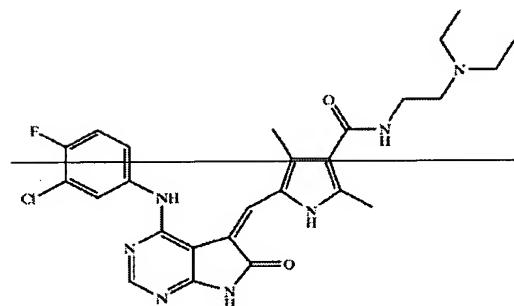
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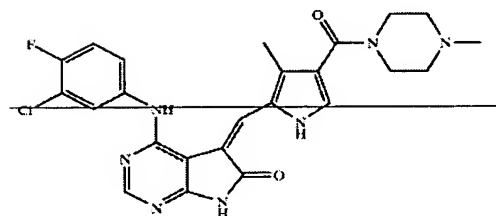
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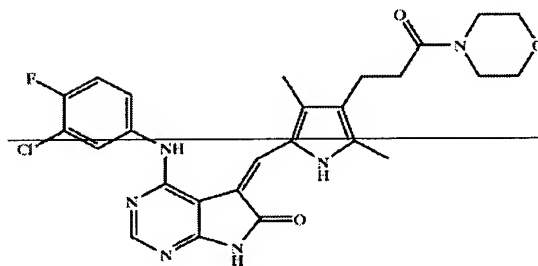
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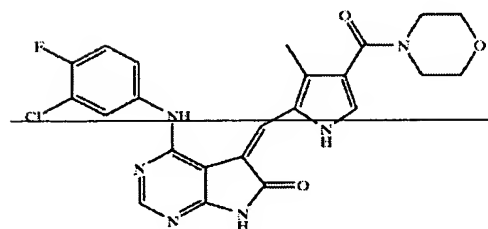
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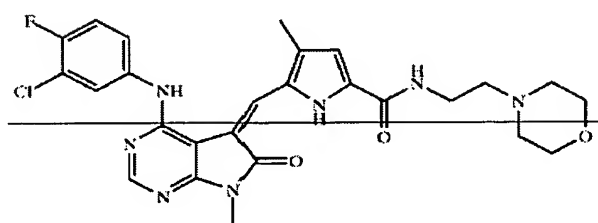
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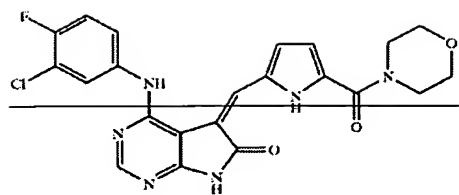
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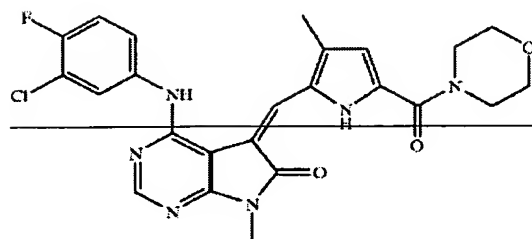
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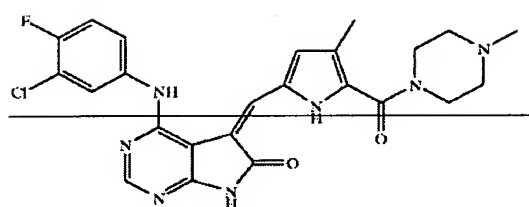
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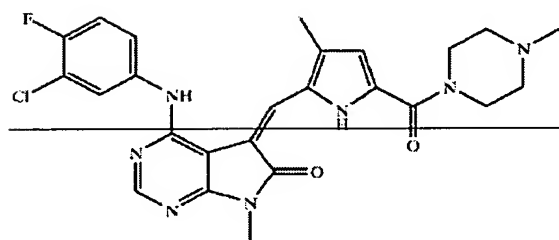
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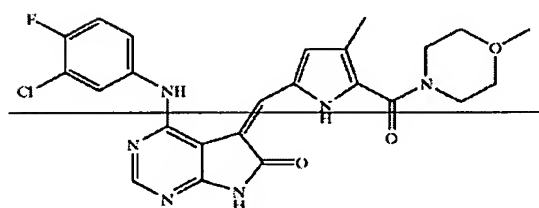
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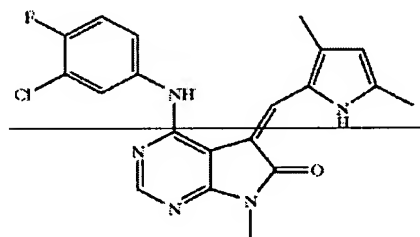
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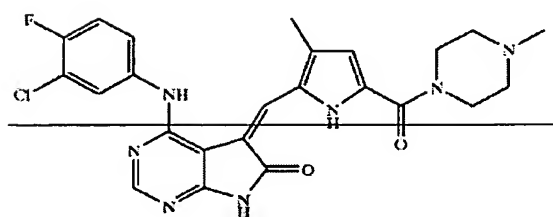
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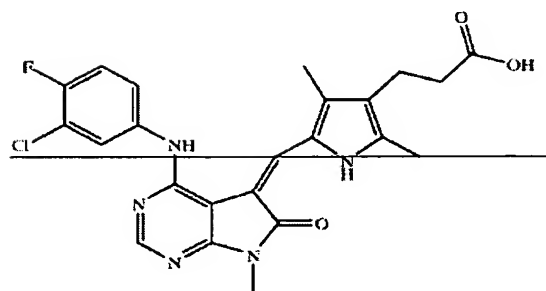
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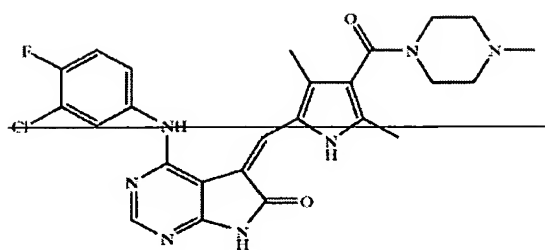
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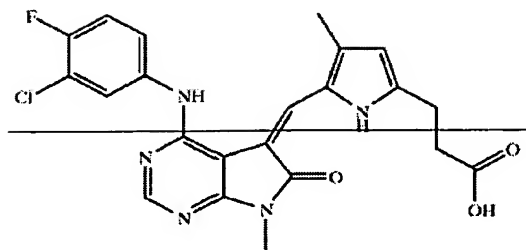
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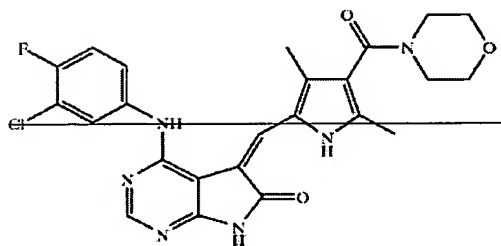
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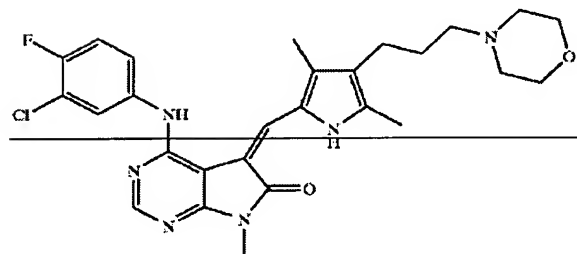
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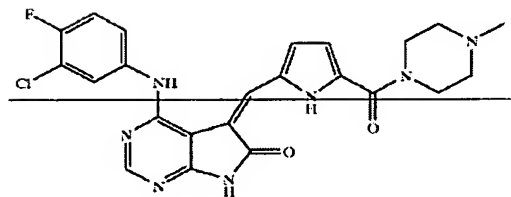
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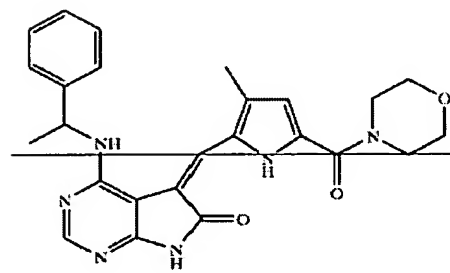
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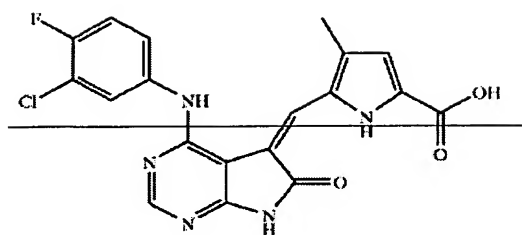
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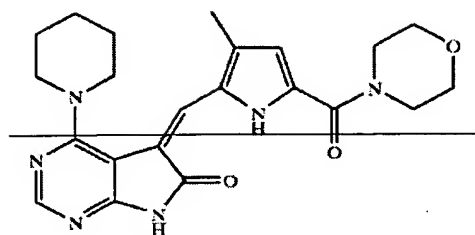
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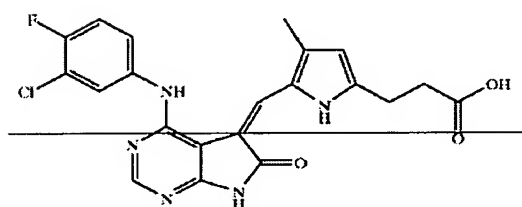
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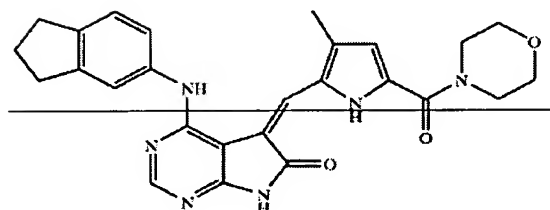
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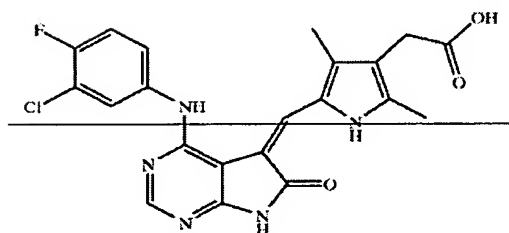
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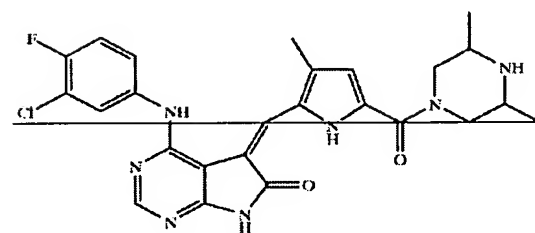
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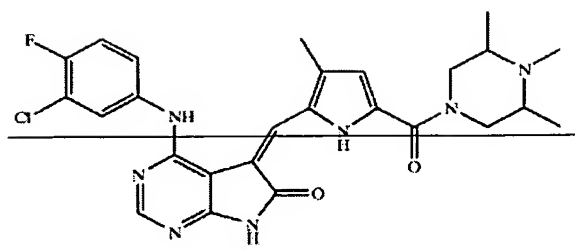
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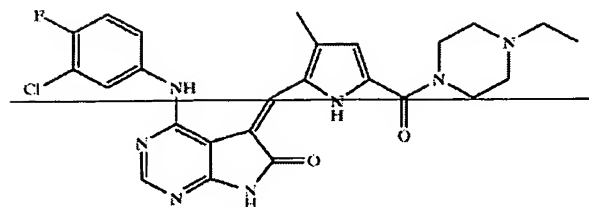
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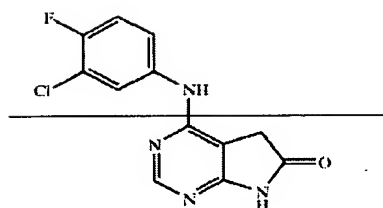
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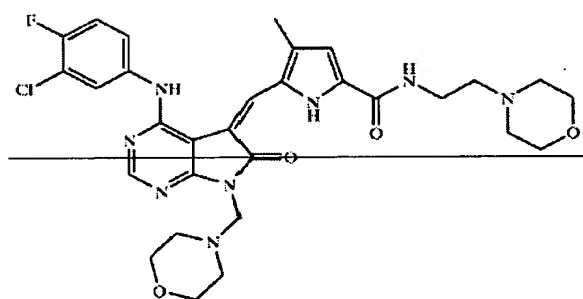
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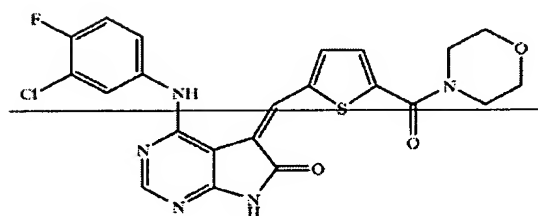
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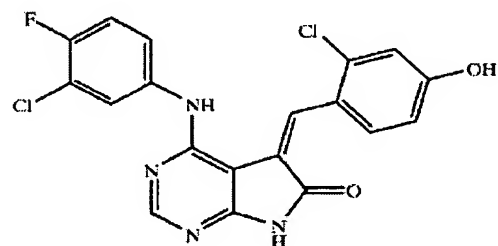
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and pharmaceutically acceptable salts, solvates, clathrates, and prodrugs thereof.

Claims 12 – 21 (Cancelled).

22. (Original) A pharmaceutical composition comprising a compound of Formula 1, or a pharmaceutically acceptable salt, solvate, clathrate, or prodrug thereof, and a pharmaceutically acceptable carrier.

23. (Original) The pharmaceutical composition comprising a compound of claim 11 and a pharmaceutical acceptable carrier or excipient.

24. (Original) The pharmaceutical composition of claim 22 which is suitable for oral, transdermal, topical, parenteral, or mucosal administration.

25. (Original) A method of regulating, modulating, or inhibiting protein kinase activity which comprises contacting a compound of Formula 1, or a pharmaceutically acceptable salt or solvate thereof, with a protein kinase.

26. (Original) The method of claim 25 wherein the protein kinase is a protein tyrosine kinase.

27. (Original) The method of claim 25 wherein the protein kinase is selected from the group consisting of abl, ATK, bcr-abl, Blk, Brk, Btk, c-fms, c-kit, c-met, c-src, CDK1, CDK2, CDK4, CDK6, cRaf1, CSF1R, CSK, EGFR, ErbB2, ErbB3, ErbB4, ERK, Fak, fes, FGFR1, FGFR2, FGFR3, FGFR4, FGFR5, Fgr, FLK-4, flt-1, Fps, Frk, Fyn, GSK, Gst-Flk1, Hck, Her-2, Her-4, IGF-1R, INS-R, Jak, JNK, KDR, Lck, Lyn, MEK, p38, PANHER, PDGFR, PLK, PKC, PYK2, Raf, Rho, ros, SRC, tie₁, tie₂, TRK, UL97, VEGFR, Yes, and Zap70.

28. (Original) The method of claim 27 wherein the protein kinase is selected from the group consisting of PANHER, EGFR, Her-2, Her-4, PDGFR, SRC, Lck, cdk2, p38, Raf, and Rho.

29. (Original) The method of claim 28 wherein the protein kinase is selected from the group consisting of PANHER, CDK2, PDGFR, p38, and Raf.

30. (Original) The method of claim 25 wherein the protein kinase is in a cell culture.

31. (Original) The method of claim 25 wherein the protein kinase is in a mammal.

32. (Original) A method of treating or preventing a mammalian disease characterized by unregulated protein kinase activity which comprises administering to a mammal in need of such treatment or prevention a therapeutically or prophylactically effective amount of a compound of Formula 1, or a pharmaceutically acceptable salt, solvate, clathrate, or prodrug thereof.

33. (Original) The method of claim 30 wherein the disease characterized by unregulated protein kinase activity is selected from the group consisting of: blood vessel proliferative disorders; fibrotic disorders; mesangial cell proliferative disorders; metabolic disorders; allergies; asthma; thrombosis; nervous system diseases; and cancer.

34. (Original) The method of claim 31 wherein the disease characterized by unregulated protein kinase activity is cancer.

35. (Original) The method of claim 32 wherein the cancer is selected from the group consisting of breast, stomach, ovary, colon, lung, brain, larynx, lymphatic system, genitourinary tract (including bladder and prostate), ovarian, gastric, bone, and pancreatic cancer.